

REMARKS***Rejection of Claims 48-54 and 56-71 Under 35 U.S.C. §102(e)***

Claims 48-54 and 56-71 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by Gunderson (USPA 20030207295; USSN 10/264,574).

Applicants respectfully traverse the rejection. As previously submitted, the Gunderson '574 application does not describe or disclose each and every step of the rejected claims.

The Gunderson '574 application was involved in Interference No. 105,547 with Applicants' U.S. Patent No. 6,858,412 ("the '412 patent"). Applicants refer the Examiner to the record in Interference No. 105,547, wherein Gunderson argued that its application disclosed inventions claimed in the '412 patent.

In the interference, Applicants have shown that Gunderson's '574 application does not describe the methods recited in the copied claims, because the Gunderson '574 application describes fundamentally different processes than were claimed in Applicants' '512 patent.

As in the claims in the '412 patent in interference, the instant claims recite a process wherein a closed circular probe is formed, the circular probe is cleaved, the cleaved probe is amplified, and then the amplicons of the amplified cleaved closed circular probe are detected. The Gunderson '574 application does not disclose the presently claimed methods. In particular, the Gunderson '574 application fails to provide supporting disclosure for, among other things, cleavage of a closed circular probe, amplification of the resulting cleaved probes, or detection of amplicons of the cleaved probe in a process such as that of the instant claims.

Claim 48 as currently presented recites:

A method of detecting one or more nucleic acid target sequences in a sample, the method comprising the steps of:

forming one or more closed circular probes whenever a first targeting domain and a second targeting domain of any of a plurality of precircle probes hybridize with their respective first target domains and second target domains of the one or more target sequences such that 5' and 3' nucleotides of the respective precircle probes abut one another, each precircle probe further having at least a first universal primer site and a cleavage site;

cleaving the one or more closed circular probes to form cleaved probes;

amplifying cleaved probes using a first universal primer complementary with a first universal primer site to form one or more amplicons; and

detecting the amplicons to detect the one or more nucleic acid target sequences in the sample.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). The elements must be arranged as required by the claim. *In re Bond*, 910 F.2d 831, 15 U.S.P.Q.2d 1566 (Fed. Cir. 1990).

The Examiner has not shown that the Gunderson '574 application discloses every element of the presently claimed methods. On page 6 of the Office Action, the Examiner has indicated paragraphs of the '574 application that are alleged to describe the formation of a closed circular probe, amplification of a probe using a universal primer, and detection of amplicon. Notably absent is any indication of a paragraph in the Gunderson '574 application that is even alleged to disclose the step "cleaving the one or more closed circular probes to

form cleaved probes.” The Gunderson ‘574 application does not even suggest such a step. Consequently, none of the paragraphs referenced as allegedly disclosing the subsequent steps actually refer to amplification of cleaved probes or detection of amplicons produced by amplifying the cleaved probe.

Gunderson only describes amplifying a closed circular probe by rolling circle amplification (RCA). By its nature, RCA requires a closed circular probe, and cannot be performed on a cleaved circular probe.

The only cleavage described by Gunderson in a method using a closed circular probe is cleaving the product of the rolling circle amplification (RCA). The product of RCA is a linear DNA. Thus, cleavage of the product of RCA cannot be confused with a step corresponding to cleaving a closed circular probe. See, e.g., Gunderson '574, para. 0182 ("Thus, in a preferred embodiment the OLA/RCA is performed in solution followed by restriction endonuclease cleavage of the RCA product." emphasis added); see also Fig. 6 and para. 0064 (illustrating OLA/RCA and the single stranded linear product of amplification of the probe (58)).

Cleavage of the linear product of an RCA process is not cleavage of a closed circular probe. No such step is cited or identified in the outstanding rejection. Accordingly, the rejection fails to support a prima facie case of anticipation, and the rejection should be withdrawn.

Similarly, applicants reject any notion that the circular probe of the RCA process is inherently cleaved by the process described by Gunderson. In order for a disclosure to be inherent, the missing descriptive matter must necessarily be present in the specification such that one of skill in the art would have recognized such a disclosure. Further, to provide "inherent" support for an affirmative limitation (e.g., cleaving a closed circular probe), the

"inherent limitation must be the 'necessary and only reasonable construction' to be given the disclosure by one skilled in the art." Langer and Tornqvist v. Kaufman and McMullen, 175 USPQ 172, 174 (CCPA 1972) citations omitted.

Cleavage of the RCA amplification product as described by Gunderson would not necessarily result in cleavage of the original probe, and thus would not inherently comprise a cleavage step as that step is recited in the instant claims. There has been no showing to the contrary. Therefore, cleavage of a closed circular probe is not an inherent property of the methods disclosed by Gunderson.

Furthermore, since there is no teaching or suggestion of cleaving a closed circular probe in any method taught by Gunderson, there cannot be any teaching or suggestion of the steps that follow cleaving the closed circular probe in the present claims, in which the cleaved probe is amplified and detected. Each of the steps of the present claims recites action upon the product of the preceding step so that any anticipating disclosure would have to disclose such steps performed in the sequence recited.

Any disclosure alleged to anticipate claim 48 and its dependent claims would have to, at least, disclose amplifying cleaved probes produced by cleaving closed circular probes. The paragraphs of the Gunderson '574 application related to amplification that have been cited in the outstanding rejection do not teach or suggest amplifying cleaved probes produced by cleaving closed circular probes.

Any disclosure alleged to anticipate claim 48 and its dependent claims would have to, at least, disclose a method comprising detection of amplicons produced by amplifying a cleaved circular probe. The paragraphs and original claims of the Gunderson '574 application related to detection of amplicons that have been cited in the outstanding rejection

do not teach or suggest detection of amplicons produced by amplifying a cleaved circular probe.

Moreover, Applicants respectfully direct the Examiner to Interference No. 105,547, in which the Board of Patent Appeals and Interferences agreed that the Gunderson '574 application did not expressly or inherently disclose a process which would necessarily result in cleavage of the closed circular probe (as posited by the Examiner in the present application). Applicants direct the Examiner's attention in particular to Paper No. 65 in Interference No. 105,547.

For at least the foregoing reasons, the Gunderson '574 application does not disclose every element of the instant claims, either explicitly or inherently, and so it could not have anticipated the instant claims. Reconsideration and withdrawal of that rejection are respectfully requested.

Rejection of Claim 55 Under 35 U.S.C. § 103(a)

Claim 55 is rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Gunderson and further in view of Carter *et al.* (1971).

The rejection of claim 55 relies upon Gunderson as allegedly teaching all the elements of the claims from which claim 55 depends and digesting using exonucleases. Carter has been cited only for allegedly teaching denaturing an exonuclease. Carter *et al.* does not remedy the deficiencies of Gunderson that have been shown above. Thus, Gunderson and Carter *et al.*, taken together, do not teach or suggest all the elements of claim 55. Accordingly, reconsideration and withdrawal of the rejection of claim 55 are respectfully requested.

CONCLUSION

In view of the above remarks, Applicants respectfully submit that the application is in condition for allowance. If the Examiner believes that a telephone call would be useful in expediting the allowance of the application, the Examiner is invited to contact the undersigned.

Applicant believes that no fee is due for the response other than the fees provided for on the accompanying transmittal. However, if an additional fee is due, please charge Deposit Account No. 50-3655, from which the undersigned is authorized to draw, under order number AFFY-201-102.

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Respectfully submitted,

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